CLAIMS

- 1. A conjugate of (1) at least one therapeutic agent for joint diseases and (2) hyaluroic acid, a hyaluroic acid derivative or a salt thereof.
- 2. The conjugate of claim 1, wherein the bond between at least one therapeutic agent for joint diseases and hyaluroic acid, a hyaluroic acid derivative or a salt thereof is a covalent bond.
- 3. The conjugate of claim 1 or 2, wherein the therapeutic agent for joint diseases is a matrix metalloprotease inhibitor.
- 4. The conjugate of any one of claims 1 to 3, wherein the matrix metalloprotease inhibitor binds to hyaluroic acid, a hyaluroic acid derivative or the salt thereof via a spacer.
- 5. The conjugate of any one of claims 1 to 4, wherein the weight ratio of the matrix metalloprotease inhibitor to the entire conjugate is 0.01 to 50%.
- 6. The conjugate of any one of claims 1 to 5, wherein the matrix metalloprotease inhibitor is a hydroxamic acid residue.
- 7. The conjugate of any one of claims 1 to 6, wherein the matrix metalloprotease inhibitor is a hydroxamic acid residue represented by the general formula (1):

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wherein

R₁ is a hydrogen atom, a hydroxyl group or a straight-chain or branched-chain alkyl group having 1 to 8 carbon atoms;

R₂ is a straight-chain or branched-chain alkyl group having 1 to 8 carbon atoms;

 R_3 is a straight chain or branched alkyl group having 1 to 8 carbon atoms which may be substituted with a cycloalkyl group, an aryl group or a heterocyclic group; and

 R_4 is a hydrogen atom or an alkyl group having 1 to 4 carbon atoms.

8. The conjugate of any one of claims 1 to 7, wherein the spacer is represented by the general formula (2):

$$-R_5 - R_6 - R_7 - R_8 -$$
 (2)

wherein

R₅ is a straight-chain or branched-chain alkylene group having 1 to 8 carbon atoms;

R₆ is an oxygen atom or a methylene or imino group which may be substituted with a straight-chain or branched-chain alkyl group having 1 to 4 carbon atoms;

 R_7 is a straight-chain or branched-chain alkylene group having 1 to 10 carbon atoms into which one to three oxygen atoms may be inserted; and R_8 is an oxygen atom, a sulfur atom or NR, wherein R, is a hydrogen atom or a straight-chain or branched-chain alkyl group having 1 to 4 carbon atoms.

9. The conjugate of any one of claims 1 to 8, wherein the conjugate of the matrix metalloprotease inhibitor and the spacer is represented by the general formula (3):

wherein

R₁₂ is a straight-chain or branched-chain alkylene group having 2 to 23 carbon atoms into which one imino group and/or one to four oxygen atoms may be inserted; and

 R_{13} is a hydrogen atom or a straight-chain or branched-chain alkyl group having 1 to 4 carbon atoms.

10. The conjugate of any one of claims 1 to 9, wherein the matrix metalloprotease inhibitor in the form of a conjugate with hyaluroic acid, a hyaluroic acid derivative or a salt thereof inhibits a matrix metalloprotease in situ.

11. A method for preparing the conjugate of any one of

11. A method for preparing the conjugate of any one of claims 1 to 10 comprising binding a site of the therapeutic agent for joint diseases that does not affect the activity of the agent to a carboxyl group, a hydroxyl group or a

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functional group at the reducing end of hyaluroic acid, a hyaluroic acid derivative or a salt thereof by direct chemical reaction or via a spacer.

- 12. A pharmaceutical composition comprising the conjugate of any one of claims 1 to 10.
- 13. The pharmaceutical composition of claim 12 which is a therapeutic agent for joint disease.
- 14. The pharmaceutical composition of c<u>laim</u> 13, wherein the joint disease is osteoarthritis, rheumatoid arthritis or scapulohumeral periarthritis.
- 15. The use of the conjugate of any one of claims 1 to 10 in the preparation of a pharmaceutical composition.
- 16. The use of the conjugate of any one of claims 1 to 10 in the preparation of a therapeutic agent for joint diseases.
- 17. A method for treating a patient having a joint disease comprising administering a pharmaceutical composition containing a pharmaceutically effective amount of the conjugate of any one of claims 1 to 10 as the effective ingredient to the patient.

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